Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-138 are pending in this application and are rejected on various grounds. All pending claims have been amended to remove references to "Figures". Claims 119-123 have been amended with the functional recitation "wherein, said encoded polypeptide induces chondrocyte redifferentiation" support for which is found in the instant specification in Example 159. Further, new claims 138-143 which recite the functional recitation "wherein, said encoded polypeptide stimulates endothelial cell proliferation" have been added, support for which is also found in the instant specification in Example 149. Claims 127-128 and 132-134 have been canceled without prejudice of disclaimer. Accordingly, Claims 119-126, 129-131, 135-143 are currently pending in this application and rejections to these claims are respectfully traversed.

Specification

The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections. Further, any minor errors have been amended.

Accordingly, Applicants believe that all objections to the specification has been overcome.

Priority

Applicants agree with the Examiner that the effective filing date for the presently claimed nucleic acids is 07/26/1999.

The Examiner had mentioned that the benefit claim to US Provisional Applications 60/213,637 filed 6/23/2000 and 60/230,978 filed 9/7/2000 were improper. Applicants agree with the Examiner's analysis and withdraw these priority claims.

Applicants submit that they rely on the "chondrocyte redifferentiation assay" for patentable utility in this case. This utility was first disclosed in International Application PCT/US00/08439, filed March 30, 2000, priority to which has been claimed in this application.

Further, Applicants also rely on the "stimulation of endothelial cell growth assay" for patentable utility in this case. This utility was first disclosed in US Provisional Application 60/145,698, filed July 26, 1999, priority to which has been claimed in this application.

Claim Rejections – 35 U.S.C. § 102

Claims 119, 120, 132-135, 137 are rejected under 35 U.S.C. §102(a or b) as being anticipated by Strausberg (dated 1/4/1999).

In view of the cancellation of claims 132-134, this rejection to these claims is moot. Strausberg describes a sequence with an overall sequence identity of 28.19% to SEQ ID NO: 371. Therefore, Strausberg does not anticipate the invention as claimed in the currently pending claims 119, 120, 135 and 137. Accordingly, this rejection should be withdrawn.

Claims 119-135, 137 are rejection under 35 U.S.C. §102(f) because the applicant did not invent the claimed subject matter because "Applicants purchased the clone containing the cDNA insert." Applicants traverse this rejection.

As indicated in the specification on page 497, Applicants determined the consensus sequence of a cDNA clone using cluster analysis and designated this clone as DNA56748. Sequence homology was determined between the DNA56748 consensus sequence and a sequence encompassed within the Incyte EST clone 3476792, which was then purchased and sequenced. Prior to the Applicants activities, the Incyte EST clone was not enabled for any function, nor was any determination done regarding any cDNA contained within, its cDNA boundaries, or utilities. Utility and function for this cDNA was entirely determined due to the Applicants activities. Hence, this rejection is improper and should be withdrawn.

Claim Rejections - 35 U.S.C. § 112, first paragraph

Claims 119-123, 132-138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a polypeptide encoding a polypeptide having at least 80% identity to a polypeptide comprising the amino acid sequence of SEQ ID NO: 371, etc. does not reasonably provide enablement for a polynucleotide encoding a polypeptide without regard to the functional activity of the encoded polypeptide.

The pending claims recite functional recitations "wherein said encoded polypeptide induces chondrocyte redifferentiation" and "wherein said encoded polypeptide stimulates endothelial cell proliferation."

PRO1186 polypeptides have utility based on results in chondrocyte redifferentiation assay

Applicants rely on the chondrocyte redifferentiation assay (Example 159) for support of patentable utility.

It was well known at the effective filing date of the present application that chondrocytes play a key role in the synthesis and maintenance of the articular cartilage, which in turn is essential to normal joint function. Unfortunately, compared to many other tissues, articular cartilage essentially lacks the ability to regenerate following injury. One way of achieving cartilage repair, for example in osteoarthritis, is to harvest human articular chrondrocytes (HACs) from non-affected, healthy areas of the joint to be repaired. The HACs are subsequently grown in monolayer cell culture in order to produce sufficient amount of cells to fill the articular defect. Chondrocytes found in healthy joints have a round shape, and express high levels of extracellular matrix molecules, such as aggrecan, type II collagen, and link protein. In contrast, monolayer cultures of chondrocytes produce dedifferentiated fibroblast-like structures, similar to those found in the cartilage of aging and arthritic joints. (See, e.g. Zhang et al., *Experimental Cell Research* 263:33-42 (2001) – copy enclosed). Accordingly, agents that are capable of inducing chondrocyte proliferation and redifferentiation, as evidenced by proper growth and differentiation of chrondrocytes in monolayer cell cultures, can be used in the treatment of joint diseases using a tissue engineering approach (See, e.g. Schnabel et al., Osteoarthritis and Cartilage, 10(1):62-70 (2002) – copy enclosed). In addition, molecules capable of inducing chondrocyte proliferation and/or redifferentiation are promising drug candidates to repair aging or arthritic joints, for example, in joints where the chondrocytes have been dedifferentiated.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The logic underlying the asserted utility in the present case is not inconsistent with general knowledge in the art, and would be considered credible by a person skilled in the art. It

is, of course, always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Applicants refer to the statement in Example 159, the description of the chondrocyte redifferentiation assay that "A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control." Fluorescence determination wherein the readout is compared to controls is well known in the art. Thus, these indica are truly determinative of the proliferation of chondrocyte cells.

Applicants respectfully submit that the specification provides sufficient disclosure to establish a specific, substantial and credible utility for the PRO1186 polypeptide and its encoding nucleic acids. In addition, the instant claims, as amended, (and, as a consequence, those claims dependent from the same) now recite the functional recitation, namely that the encoded polypeptide induces chondrocyte re-differentiation.

Accordingly, Applicants respectfully submit that it would not require undue experimentation for one of skill in the art to apply the teachings of the present disclosure so as to practice the invention of the instant claims (and, as a consequence, those claims dependent from the same).

PRO1186 polypeptides also have utility based on results in the stimulation of endothelial cell proliferation

As asserted by the applicants in this assay, polypeptides testing positive in this assay are useful for the therapeutic treatment of conditions or disorders where angiogenesis is necessary, for example, in wound healing, etc. Antagonists developed to this polypeptide is useful in inhibiting angiogenesis in conditions like tumor growth, etc. Based on a positive reaction in this assay, and the specific, substantial and credible utility, and the instant disclosureand since the claims are now drawn to a genus of nucleotides defined both by sequence and functional identity, one skilled in the art at the effective priority date would know how to make and use the nucleic acid of SEQ ID NO:370 and PRO1186 (SEQ ID NO:371) based on the asserted utilities.

Therefore, this rejection should be withdrawn.

Claim Rejections - 35 U.S.C. § 112, first paragraph -written description

Claims 119-123, 132-138 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

Firstly, these rejections are moot for claims 132-134 in view of their cancellation. Further, as discussed above, specific utilities have now been asserted for the presently pending claims based on functional recitations "wherein said encoded polypeptide induces chondrocyte redifferentiation" and "wherein said encoded polypeptide stimulates endothelial cell proliferation." Since the claims are now drawn to a genus of nucleotides defined both by sequence and functional identity, it would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the nucleic acid of SEQ ID NO:370 and PRO1186 (SEQ ID NO:371), that the Applicant possessed these obvious variations and adaptations of SEQ ID NO:371 at the time of filing.

Hence, Applicants request that the present rejection be reconsidered and withdrawn.

Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 119-124, 127, 128, 132-138 were rejected under 35 U.S.C. §112, second paragraph for being indefinite. The Examiner alleges that the protein identified as PRO1186 is not disclosed as being expressed on a cell surface and accordingly, claims that recite an "extracellular domain" is indefinite as the art does not recognize soluble proteins as having such domains. The Examiner further rejects Claim 133 as being indefinite for reciting "hybridizes." Applicants respectfully traverse these rejections.

Without acquiescing to the propriety of this rejection and without limitations to pursuing this subject matter in future applications, merely to expedite prosecution in this case, Applicants have canceled references to "the extracellular domain" in the pending claims and further, have canceled claims 127-128 and 132-134 without prejudice or disclaimer. Accordingly, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C65). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: December 10, 2004

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